

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Kirill Ostanin, *et al.*

Serial No.: Not Assigned

Filed: December 1, 2003

For: *CELL SURFACE PROTEINS AND USE
THEREOF AS INDICATORS OF ACTIVATION OF
CELLULAR SIGNAL TRANSDUCTION PATHWAYS*

Attorney Docket No.: 50370-60409CON

Group Art Unit: 1646

Examiner: Li, Ruixiang

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATION UNDER 37 CFR 1.10

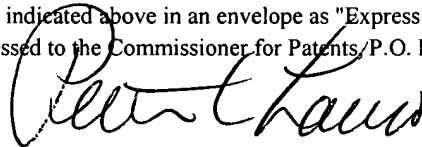
Date of Deposit: December 1, 2003

Mailing Label Number: EV 342589657 US

I hereby certify that this 37 CFR 1.53(b) request and the documents referred to as attached therein are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Peter C. Lauro, Esq.

Name of Person Mailing Paper



Signature of Person Signing

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their attorney are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. This application is a continuation application of application serial number 09/658,765, filed September 8, 2000, (the parent application) to which the instant application claims priority pursuant to 35 U.S.C. §120. The references cited on the enclosed PTO Form 1449 were cited in an Information Disclosure

Statement that was filed in the parent application on April 27, 2001 and that met the requirements of 37 C.F.R. 1.98(a)-(c). Accordingly, pursuant to 37 C.F.R. 1.98(d).

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(1), no additional costs are believed to be due in connection with the filing of this disclosure. Nevertheless, please charge any required fee or credit any overpayment to our Deposit Order Account No. 04-1105.

Respectfully submitted,

EDWARDS & ANGELL, LLP

A handwritten signature in black ink, appearing to read "Peter C. Lauro", written over a horizontal line.

Peter C. Lauro, Esq.

Registration No. 32,360

Attorney for Applicants

101 Federal Street
Boston, MA 02110
(617) 227-7400

Date: December 1, 2003

PCL/thl
Enclosures

APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO 50370-60409CON	Sheet 1 of 11 SERIAL NO. N t Assigned
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		APPLICANT Ostanin. Kirill	
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U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	4,948,874	08/90	Kronvall et al.	350	350
	A2	5,096,815	03/92	Ladner et al.	435	69.1
	A3	5,283,173	02/94	Fields et al.	435	6

FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
A4	WO 88/10308	12/88	PCT		
A5	WO 91/12273	08/91	PCT		
A6	WO 92/05244	04/92	PCT		

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

A7	Akada, R. et al. "Genetic Relationships Between the G Protein $\beta\gamma$ Complex, Ste5p, Ste20p and Cdc42p: Investigation of Effector Roles in the Yeast Pheromone Response Pathway," <i>Genetics</i> 143:103-117 (1996)
A8	Alison, Malcolm R. et al. "Growth factors and growth factor receptors," <i>Brit. J. of Hosp. Med.</i> 49(11):774-88 (1993)
A9	Altieri, Dario C. "Proteases and protease receptors in modulation of leukocyte effector functions," <i>J. of Leukocyte Biol.</i> 58:120-27 (1995)
A10	Artemyev, Nikolai O. et al. "Sites of Interaction between Rod G-Protein α -Subunit and cGMP-phosphodiesterase γ -Subunit," <i>J. Biol. Chem.</i> 267(35):25067-72 (1992)
A11	Awramik, S. M. "New fossil finds in old rocks," <i>Nature</i> 319:446-47 (1986)
A12	Belka, C. et al. "The role of tyrosine kinases and their substrates in signal transmission of hematopoietic growth factors: a short review," <i>Leukemia</i> 9:754-61 (1995)
A13	Bender, Alan and Sprague, George F. Jr. "Pheromones and Pheromone Receptors Are the Primary Determinants of Mating Specificity in the Yeast <i>Saccharomyces cerevisiae</i> ," <i>Genetics</i> 121:463-76 (1989)
A14	Birnbaumer, Lutz "Transduction of receptor signal into modulation of effector activity by G proteins: the first 20 years or so..." <i>FASEB Journal</i> 4:3178-88 (1990)
A15	Blinder, Dmitry et al. "Constitutive Mutants in the Yeast Pheromone Response: Ordered function of the Gene Products," <i>Cell</i> 56:479-486 (1989)
A16	Brill, Julie A. et al. "A Role for Autophosphorylation Revealed by Activated Alleles of <i>FUS3</i> , the Yeast MAP Kinase Homolog," <i>Molecular Biology of the Cell</i> 5:297-312 (1994)
A17	Brugarolas, James et al. "Radiation-induced cell cycle arrest compromised by p21 deficiency," <i>Nature</i> 377:522-57 (1995)
A18	Burack, W. Richard et al. "The Activating Dual Phosphorylation of MAPK by MEK Is Nonprocessive," <i>Biochemistry</i> 36(20):5929-5933 (1997)

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Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	B1	5,401,629	03/95	Harpold et al.	435	6	
	B2	5,436,128	07/95	Harpold et al.	435	6	
	B3	5,468,614	11/95	Fields et al.	435	6	

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							YES	NO
	B4	WO 92/08740	05/92	PCT				
	B5	WO 93/10230	05/93	PCT				
	B6	EP 568,925	11/93	EPO				

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	B7	Cavallini, Bruno et al. "A yeast activity can substitute for the HeLa Cell TATA box factor," <i>Nature</i> 334:77-80 (1988)
	B8	Chambers, D. A. et al. "Neuroimmune Modulation: Signal Transduction and Catecholamines," <i>Neurochem. Int.</i> 22(2):95-110 (1993)
	B9	Chan, Russell K. and Otte, Carol A. "Isolation and Genetic Analysis of <i>Saccharomyces cerevisiae</i> Mutants Supersensitive to G1 Arrest by a Factor and α Factor," <i>Molecular and Cellular Biol.</i> 2(1):11-20 (1982)
	B10	Chang, Fred and Herskowitz, Ira "Identification of a Gene Necessary for Cell Cycle Arrest by a Negative Growth Factor of Yeast: FAR1 is an Inhibitor of a G1 Cyclin, CLN2," <i>Cell</i> 63:999-1011 (1990)
	B11	Chien, Cheng-Ting, et al. "The two-hybrid system: A method to identify and clone genes for proteins that interact with a protein of interest," <i>Proc. Natl. Acad. Sci. USA</i> 88:9578-82 (1991)
	B12	Clark, Karen L. et al. "Interactions among the Subunits of the G-protein Involved in <i>Saccharomyces cerevisiae</i> Mating," <i>Molecular and Cellular Biol.</i> 13(1):1-8 (1993)
	B13	Cole, Gary M. et al. "Stoichiometry of G Protein Subunits Affects the <i>Saccharomyces cerevisiae</i> Mating Pheromone Signal Transduction Pathway," <i>Molecular and Cellular Biology</i> 10(2):510-517 (1990)
	B14	Coleman, David E. et al. "Structures of Active Conformation of $G_{i\alpha 1}$ and the Mechanism of GTP Hydrolysis," <i>Science</i> 265:1405-12 (1994)
	B15	Conklin, Bruce R. et al. "Substitution of three amino acids switches receptor specificity of $G_{q\alpha}$ to that of $G_{i\alpha}$," <i>Nature</i> 363:274-76 (1993)
	B16	Cwirla, Steven E. et al. "Peptides on phage: A vast library of peptides for identifying ligands," <i>Proc. Natl. Acad. Sci. USA</i> 87:6378-82 (1990)
	B17	Devlin, James J. et al. "Random Peptide Libraries: A Source of Specific Protein Binding Molecules," <i>Science</i> 249:404-6 (1990)
	B18	Dietzel, Christine and Kurjan, Janet "The Yeast SCG1 Gene: A $G\alpha$ -like Protein Implicated in the α - and α -Factor Response Pathway," <i>Cell</i> 50:1001-10 (1987)

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	C1	5,580,736	12/96	Brent et al.	435	6	
	C2	5,691,188	11/97	Pausch et al.	435	225.1	

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							YES	NO
	C3	WO 94/23025	10/94	PCT				
	C4	WO 95/30012	11/95	PCT				
	C5	WO 97/11159	03/97	PCT				
	C6	WO 98/13513	04/98	PCT				

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	C7	Dmochowska, Aleksandra et al. "Yeast <i>KEX1</i> Gene Encodes a Putative Protease with a Carboxypeptidase B-like Function Involved in Killer Toxin and α -Factor Precursor Processing," <i>Cell</i> 50:573-84 (1987)
	C8	Dolan, J. W. et al. "Overproduction of the yeast STE12 protein leads to constitutive transcriptional induction," <i>Genes & Development</i> 4(4):492-502 (1990)
	C9	Dubois, Patrice M. et al. "Role of the transmembrane and cytoplasmic domains of surface IgM in endocytosis and signal transduction," <i>Eur. J. Immunol.</i> 22:851-57 (1992)
	C10	Erickson, Deborah "Intercepted Messages: New biotechnology drugs target intracellular communication," <i>Scientific American</i> 267(5):122-23 (1992)
	C11	Etienne, Gilles et al. "A Screening Method for Antifungal Substances Using <i>Saccharomyces cerevisiae</i> Strains Resistant to Polyene Macrolides," <i>J. of Antibiotics</i> 43(2):199-206 (1990)
	C12	Fasullo, Michael T. and Davis, Ronald W. "Direction of Chromosome Rearrangements in <i>Saccharomyces cerevisiae</i> by Use of <i>his3</i> Recombination Substrates," <i>Molecular and Cellular Biol.</i> 8(10):4370-80 (1988)
	C13	Ferrell, James E. Jr. et al. "The Biochemical Basis of an All-or-None Cell Fate Switch in <i>Xenopus</i> Oocytes," <i>Science</i> 280:895-898 (1998)
	C14	Ferrell, James E. Jr. "Tripping the switch fantastic: how a protein kinase cascade can convert graded inputs into switch-like outputs," <i>Trends In Biochem. Sci.</i> 21(12):460-6 (1996)
	C15	Fields, Stanley and Song Ok-kyu "A novel genetic system to detect protein-protein interactions," <i>Nature</i> 340:245-46 (1989)
	C16	Franke, Arthur E. et al. "Human C5a Anaphylatoxin: Gene Synthesis, Expression, and Recovery of Biologically Active Material from <i>Escherichia coli</i> ," <i>Methods in Enzymology</i> 162:653-68 (1988)
	C17	Funaro, Ana et al. "Human CD38 is associated to distinct molecules which mediate transmembrane signaling in different lineages," <i>Eur. J. Immunol.</i> 23:2407-11 (1993)
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D1	Gallego, Carme et al. "Myristoylation of the G _{o12} polypeptide, a G protein α subunit, is required for its signaling and transformation functions," <i>Proc. Natl. Acad. Sci. USA</i> 89:9695-99 (1992)
D2	Garritsen, Anja et al. "The N-Terminal coiled-coil domain of β is essential for γ association: A Model for G-Protein $\beta\gamma$ subunit interaction," <i>Proc. Natl. Acad. Sci. USA</i> 90:7706-10 (1993)
D3	Gerard, Norma P. and Gerard, Craig "Construction and Expression of a Novel Recombinant Anaphylatoxin, C5a-N19, a Probe for the Human C5a Receptor," <i>Biochemistry</i> 29(39):9274-81 (1990)
D4	Gordon, J. "B-cell signaling via the C-type lectins CD23 and CD72," <i>Immunology Today</i> 15(9):411-17 (1994)
D5	Graf, Rolf et al. "A Truncated Recombinant α Subunit of G ₁₃ with a Reduced Affinity for $\beta\gamma$ Dimers and Altered Guanosine 5'-3-O-(Thio)triphosphate Binding," <i>J. of Biol. Chem.</i> 267(34):24307-14 (1992)
D6	Gros, Philippe et al. "Mammalian Multidrug Resistance Gene: Complete cDNA Sequence Indicates Strong Homology to Bacterial Transport Proteins," <i>Cell</i> 47:371-80 (1986)
D7	Gyuris, Jenő et al. "Cdi1, A Human G1 and S Phase Protein Phosphatase That Associates with Cdk2," <i>Cell</i> 75:791-803 (1993)
D8	Hagen, David C. et al. "Evidence the yeast STE3 gene encodes a receptor for the peptide pheromone a factor: Gene sequence and implications for the structure of the presumed receptor," <i>Proc. Natl. Acad. Sci. USA</i> 83:1418-22 (1986)
D9	Hall, Marcia et al. "Evidence for different modes of action of cyclin-dependent kinase inhibitors: p15 and p16 bind to kinases, p21 and p27 bind to cyclins," <i>Oncogene</i> 11:1581-88 (1995)
D10	Harbury, Pehr B. et al. "A Switch Between Two-, Three- and Four-Stranded Coiled Coils in GCN4 Leucine Zipper Mutants," <i>Science</i> 262:1401-07 (1993)
D11	Hartwell, Leland H. "Mutants of <i>Saccharomyces cerevisiae</i> Unresponsive to Cell Division Control by Polypeptide Mating Hormone," <i>J. Cell Biol.</i> 85:811-22 (1980)
D12	Hasson, M.S. et al. "Mutational Activation of the STE5 Gene Product Bypasses the Requirement for G Protein β and γ Subunits in the Yeast Pheromone Response Pathway," <i>Molecular and Cellular Biology</i> 14(2):1054-1065 (1994)
D13	He, Bin et al. "RAM2, an essential gene of yeast, and RAM1 encode the two polypeptide components of the farnesyltransferase that prenylates a-actor and Ras proteins," <i>Proc. Natl. Acad. Sci. USA</i> 88:11373-77 (1991)

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E1	Hiltunen, J. Kalervo et al. "Peroxisomal Multifunctional β -Oxidation Protein of <i>Saccharomyces cerevisiae</i> ," <i>J. of Biol. Chem.</i> 267(10):6646-6653 (1992)
E2	Hrycyna, Christine A. et al. "The <i>Saccharomyces cerevisiae</i> STE14 gene encodes a methyltransferase that mediates C-terminal methylation of a-factor and RAS Proteins," <i>The EMBO J.</i> 10(1):1699-1709 (1991)
E3	Huang, Chi-Ying F. et al. "Ultrasensitivity in the mitogen-activated protein kinase cascade," <i>Proc. Natl. Acad. Sci. USA</i> 93:10078-10083 (1996)
E4	Hughes, David A. et al. "Complementation of <i>byr1</i> in fission yeast by mammalian MAP kinase kinase requires coexpression of Raf kinase," <i>Nature</i> 364:349-52 (1993)
E5	Imamoto, Akira et al. "Genetics of signal transduction: tales from the mouse," <i>Curr. Opin. Gen. & Dev.</i> 4:40-46 (1994)
E6	Inouye, Carla et al. "Ste5 RING-H2 Domain: Role in Ste4-Promoted Oligomerization for Yeast Pheromone Signaling," <i>Science</i> 278:103-106 (1997)
E7	Jabbar, M. Abdul et al. "Influenza Viral (AWSN/33) hemagglutinin is expressed and glycosylated in the yeast <i>Saccharomyces cerevisiae</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 82:2019-23 (1985)
E8	Jakobs, K. H. et al. "Dual regulation of adenylate cyclase. A signal transduction mechanism of membrane receptors," <i>Basic Res. Cardiol.</i> 81:1-9 (1986)
E9	Journot, Laurent et al. "Amino Acids 367-376 of the G _s α subunit induce membrane association when fused to soluble amino-terminal deleted G ₁₁ α subunit," <i>Proc. Natl. Acad. Sci. USA</i> 88:10054-58 (1991)
E10	Julius, David et al. "Glycosylation and Processing of Prepro- α -Factor through the Yeast Secretory Pathway," <i>Cell</i> 36:309-18 (1984)
E11	Julius, David et al. "Isolation of the Putative Structural Gene for the Lysine-Arginine-Cleaving Endopeptidase Required for Processing of Yeast Prepro- α -factor," <i>Cell</i> 37:1075-89 (1984)
E12	Julius, David et al. "Yeast α Factor is Processed from a Larger Precursor Polypeptide: The Essential Role of a Membrane-Bound Dipeptidyl Aminopeptidase," <i>Cell</i> 32:839-52 (1983)
E13	Kaiser, Chris A. et al. "Many Random Sequences Functionally Replace the Secretion Signal Sequence of Yeast Invertase," <i>Science</i> 235:312-17 (1987)
E14	Kang, Yoon-Se et al. "Effects of expression of mammalian G α and hybrid mammalian-yeast G α proteins on the yeast pheromone response signal transduction pathway," <i>Molecular and Cellular Biology</i> 10(6):2582-90 (1990)

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F1		King, Klim et al. "Control of Yeast Mating Signal Transduction by a Mammalian β_2 -Adrenergic Receptor and $G_s \alpha$ Subunit," <i>Science</i> 250:121-23 (1990)	
F2		Kingsman, S.M. et al. "The production of mammalian protein in <i>Saccharomyces cerevisiae</i> ," <i>Tibtech</i> 5:53-57 (1987)	
F3		Koff, Andrew et al. "Human Cyclin E, a New Cyclin That Interacts with Two Members of the CDC2 Gene Family," <i>Cell</i> 66:1217-28 (1991)	
F4		Kosugi, Shinji et al. "Characterization of heterogeneous mutations causing constitutive activation of the luteinizing hormone receptor in familial male precocious puberty," <i>Human Molecular Genetics</i> 4(2):183-88 (1995)	
F5		Kramer, R. A. et al. "HTLV-III gag Protein Is Processed in Yeast Cells by the Virus pol-Protease," <i>Science</i> 231:1580-85 (1986)	
F6		Kuchler, Karl and Thorner, Jeremy "Functional expression of human <i>mdr1</i> in the yeast <i>Saccharomyces cerevisiae</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 89:2302-06 (1992)	
F7		Kuchler, Karl et al. " <i>Saccharomyces cerevisiae</i> STE6 gene product: a novel pathway for protein export in eukaryotic cells," <i>The EMBO J.</i> 8(13):3973-84 (1989)	
F8		Kurjan, Janet "α-Factor Structural Gene Mutations in <i>Saccharomyces cerevisiae</i> : Effects on α-Factor Production and Mating," <i>Molecular and Cellular Biol.</i> 5(4):787-96 (1985)	
F9		Kurjan, Janet and Herskowitz "Structure of a Yeast Pheromone Gene (<i>MFa</i>): A Putative α-Factor Precursor Contains Four Random Copies of Mature α-Factor," <i>Cell</i> 30:933-43 (1982)	
F10		Lambright, David G. et al. "Structural determinants for activation of the α-subunit of a heterotrimeric G protein," <i>Nature</i> 369:621-28 (1994)	
F11		Leberer, Ekkehard et al. "Dominant-negative mutants of a yeast G-protein β subunit identify two functional regions involved in pheromone signaling," <i>The EMBO J.</i> 11(13):4805-13 (1992)	
F12		Lee, Ethan et al. "The G22A Mutant of G_{sa} Highlights the Requirement for Dissociation of G Protein Subunits," <i>J. Biol. Chem.</i> 267(2):1212-18 (1992)	
F13		Lemire, Bernard D. et al. "The Mitochondrial Targeting Function of Randomly Generated Peptide Sequences Correlates with Predicted Helical Amphiphilicity," <i>J. Biol. Chem.</i> 264(34):20206-12 (1989)	
F14		Lew, Daniel J. et al. "Isolation of Three Novel Human Cyclins by Rescue of G1 Cyclin (Cln) Function in Yeast," <i>Cell</i> 66:1197-1206 (1991)	
F15		Linder, Maurine E. and Gilman, Alfred G. "G Proteins," <i>Scientific American</i> 267(1):56-65 (1992)	
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G1	Linder, Maurine E. et al. "Lipid Modifications of G Protein Subunits: Myristoylation of G _{0a} Increases its Affinity for $\beta\gamma$," <i>J. Biol. Chem.</i> 266(7):4654-59 (1991)
G2	Lupas, Andrei N. et al. "Do G protein subunits associate via a three-stranded coiled coil?" <i>FEBS</i> 314(2):105-08 (1992)
G3	Mackay, Vivian and Manney, Thomas R. "Mutations Affecting Sexual Conjugation and Related Processes in <i>Saccharomyces cerevisiae</i> . II Genetic Analysis of Nonmating Mutants," <i>Genetics</i> 76:273-88 (1974)
G4	Marengere, Luc E.M. and Pawson, Tony "Structure and function of SH2 domains," <i>J. Cell Science Suppl.</i> 18:97-104 (1994)
G5	Markby, David W. et al. "Separate GTP Binding and GTPase Activating Domains of a G α Subunit," <i>Science</i> 262:1895-1901 (1993)
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